FILE 'CAPLUS' ENTERED AT 16:02:28 ON 07 JUL 2003

L1 137 S SOMATOSTATIN AND ((ANIONIC POLYMER) OR POLYACRYLAMIDE OR POLY
L2 82 S L1 AND PATENT/DT
L3 55 S L1 NOT L2

=> d bib,abs 8,22,43,45,46,47,49,50,51

L3 ANSWER 8 OF 55 CAPLUS COPYRIGHT 2003 ACS
AN 1996:491324 CAPLUS
DN 125:230514
TI Nasal delivery of octreotide: Absorption enhancement by particulate carrier systems
AU Oechslein, Christine R.; Fricker, Gert; Kissel, Thomas
CS Department of Pharmaceutics and Biopharmacy, Philipps-Universitaet Marburg, Marburg, Germany
SO International Journal of Pharmaceutics (1996), 139(1,2), 25-32
CODEN: IJPHDE; ISSN: 0378-5173
PB Elsevier
DT Journal
LA English
AB The potential of various powder formulations to enhance the nasal absorption of the **somatostatin** analog peptide octreotide (Sandostatin) was studied by a combination of in vitro and in vivo expts. The particulate carriers under investigation were microcryst. **cellulose** (Avicel PH101), semicryst. **cellulose** (Elcema P050), hydroxyethyl **starch**, crosslinked dextran (Sephadex G25), microcryst. chitosan, pectin and alginic acid. Detn. of the Ca2+--binding capacity of these carriers demonstrated large differences for excipients of the same chem. compn., depending on the phys. appearance. Whereas Avicel PH101 bound 0.22 .mu.g Ca2+/mg carrier, no Ca2+ binding could be detected for Elcema P050. The following rank order was obtained: swollen Sephadex G25 > alginic acid > microcryst. **cellulose** = hydroxyethyl **starch** .mchgt. chitosan = pectin = semicryst. **cellulose** = 0. For Sephadex G25 a pre-swelling time of at least 30 min was necessary to observe calcium binding (0.55 .mu.g /mg). Detn. of water uptake by the different excipients showed a very rapid water uptake of more than 200% (wt/wt) by microcryst. chitosan and Avicel PH101. The rate and extent of water uptake can be ranked for the nasal particulate carriers as follows: chitosan > microcryst. **cellulose** > semicryst. **cellulose** .mchgt. pectin = hydroxyethyl **starch** = alginic acid = Sephadex G25. When the absorption of octreotide was detd. in vivo in rats after nasal administration together with the resp. carrier, the highest bioavailability was seen after coadministration of alginic acid and Sephadex G25 (4,1% and 5.56%). Tmax of plasma concn. was between 0.08 and 0.34 min. It was delayed after coadministration of Sephadex G25 and pectin (1 and 2 h), which might be explained by swelling time and gel formation of the excipients. The data suggest a correlation between calcium-binding properties of nasal carriers and their potential as nasal absorption enhancers for peptides under in vivo conditions.

L3 ANSWER 22 OF 55 CAPLUS COPYRIGHT 2003 ACS
AN 1988:149310 CAPLUS
DN 108:149310
TI Diet composition and the plasma levels of some peptides regulating pancreatic secretion in the pig
AU Corring, T.; Chayvialle, J. A.
CS Lab. Physiol. Nutr., INRA, Jouy-en-Josas, 78350, Fr.
SO Reproduction, Nutrition, Developpement (1980-1988) (1987), 27(6), 967-77
CODEN: RNDED4; ISSN: 0181-1916
DT Journal
LA English
AB The effects of diet compn. upon the plasma levels of peptides known to be

involved in the hormonal regulation of exocrine pancreas secretion were studied in 6 growing Large White pigs. Three pigs were fed in the following sequence: fat-rich diet for 7 days, control diet for 7 days, **starch**-rich diet for 7 days, and the other 3 pigs were fed the same diets over the same time lengths in inverse sequence. The 3 diets were isoproteinic (16% protein) and isocaloric (3850 cal/kg). Pancreatic adaptation to the diet, i.e., increase of lipase-specific activity when the pigs ingested 6 times more fat per day and an increase in amylase-specific activity when they ingested 3 times more **starch** per day, was confirmed. Changes in diet compn. did not lead to any lasting significant change in plasma peptide levels. Cholecystokinin, secretin, pancreatic polypeptide, and **somatostatin**, known to regulate exocrine pancreas secretion, apparently are not involved in the mechanisms of pancreatic amylase and lipase adaptation to the amt. of carbohydrate and fat ingested by pigs.

L3 ANSWER 43 OF 55 CAPLUS COPYRIGHT 2003 ACS
AN 1981:26218 CAPLUS
DN 94:26218
TI Cell-free synthesis of **somatostatin**
AU Oyama, Hideki; O'Connell, Keith; Permutt, Alan
CS Sch. Med., Washington Univ., St. Louis, MO, 63110, USA
SO Endocrinology (1980), 107(3), 845-7
CODEN: ENDOAO; ISSN: 0013-7227
DT Journal
LA English
AB The mRNA from catfish pancreatic islets was translated in a wheat germ cell-free protein-synthesizing system. A protein of mol. wt. 12,000, preprosomatostatin, was identified by specific immunopptn. with anti-catfish pancreatic **somatostatin** and SDS-**polyacrylamide** gel electrophoresis.

L3 ANSWER 45 OF 55 CAPLUS COPYRIGHT 2003 ACS
AN 1980:439861 CAPLUS
DN 93:39861
TI Isolation and characterization of immunoreactive **somatostatin** from fish pancreatic islets
AU Oyama, Hideki; Hirsch, Harry J.; Gabbay, Kenneth H.; Permutt, Alan
CS Dep. Med., Washington Univ. Sch. Med., St. Louis, MO, 63110, USA
SO Journal of Clinical Investigation (1980), 65(5), 993-1002
CODEN: JCINAO; ISSN: 0021-9738
DT Journal
LA English
AB Using a radioimmunoassay with labeled synthetic tetradecapeptide **somatostatin** (I), a large amt. of immunoreactive I was found in the principal pancreatic islet of the channel catfish (Ictalurus punctata). Exts. of islets were chromatog. on a Bio-Gel P-30 column, and >90% of the immunoreactive I migrated with proteins at least twice the size of synthetic tetradecapeptide I. This fraction was further purified by ion-exchange chromatog. on CM-**cellulose** and DEAE-**cellulose** columns. Two peptides were obtained with identical immunoreactivity, which was .apprx.25% that of the synthetic I. Each peptide was >95% pure by thin-layer electrophoresis, **polyacrylamide** gel electrophoresis at pH 8.9, and high-pressure liq. chromatog. Further criteria of purity included N-terminal anal. of fraction IV yielding only aspartic acid. A total of 1.3 mg of fraction II, and 3.8 mg of fraction IV I-like peptides were obtained from 10 g of fresh frozen islets. Characterization of the 2 peptides revealed both peptides to be slightly more acidic than synthetic tetradecapeptide I. Fraction II had an isoelec. point of 8.0-8.3, and fraction IV had an isoelec. point of 8.3-9.0. Mol. wt. estn. by Na dodecyl sulfate-urea **polyacrylamide** gel electrophoresis revealed similar mobility of both peptides, between pancreatic polypeptide (mol. wt. 4500) and glucagon (mol. wt. 3500). The mobility was not altered by redn., and was approx.

twice the size of synthetic tetradecapeptide I (mol. wt. 1800). This confirmed that the peptides were single polypeptide chains and not aggregates, or I bound to larger proteins. Mol. wt. detn. by gel filtration chromatog. on Bio-Gel P-6 in 8M urea gave an estd. mol. wt. of 3700. Amino acid anal. of the 2 immunoreactive I indicated that they were very similar in compn. Both pancreatic I's (1 .mu.M) had full biol. activity relative to synthetic I as measured by inhibition of growth hormone release from rat anterior pituitary cells.

L3 ANSWER 46 OF 55 CAPLUS COPYRIGHT 2003 ACS
AN 1980:193868 CAPLUS
DN 92:193868
TI A radioimmunosorbent assay for plasma **somatostatin**
AU Lundqvist, Gudmar; Gustavsson, Sven; Elde, Robert; Arimura, Akira
CS Dep. Clin. Chem. Surg., Univ. Uppsala, Uppsala, Swed.
SO Clinica Chimica Acta (1980), 101(2-3), 183-91
CODEN: CCATAR; ISSN: 0009-8981
DT Journal
LA English
AB A solid-phase radioimmunoassay for the detn. of immunoreactive **somatostatin** (IRS) in plasma is described. Plasma samples obtained from healthy persons and from anesthetized pigs were extd. with Me2CO/petroleum ether. The antibodies were conjugated to CNBr-activated microcryst. **cellulose**. Tyr1-**somatostatin** was iodinated according to the lactoperoxidase method. After extn. the recovery of **somatostatin** was 80-118%. The sensitivity of the assay was 5-10 pg/mL, and interassay variation was 8-20%. The mean value of IRS in systemic blood in man was 77 pg/mL. I.v. administration of 10 .mu.g/kg synthetic **somatostatin** to anesthetized pigs was followed by a 20-fold increase in plasma IRS. The hypersomatostatinemia rapidly vanished with a half-life of 3.5 min. The level of IRS in cerebrospinal fluid was unchanged by i.v. **somatostatin** at this dose.

L3 ANSWER 47 OF 55 CAPLUS COPYRIGHT 2003 ACS
AN 1980:74083 CAPLUS
DN 92:74083
TI Partial purification and characterization of a peptide with growth hormone-releasing activity from extrapituitary tumors in patients with acromegaly
AU Frohman, Lawrence A.; Szabo, Marta; Berelowitz, Michael; Stachura, Max E.
CS Michael Reese Med. Cent., Univ. Chicago, Chicago, IL, 60616, USA
SO Journal of Clinical Investigation (1980), 65(1), 43-54
CODEN: JCINAO; ISSN: 0021-9738
DT Journal
LA English
AB Growth hormone (GH)-releasing activity was detected in exts. of carcinoid and pancreatic islet tumors from 3 patients with GH-secreting pituitary tumors and acromegaly. Bioactivity was demonstrated in 2N acetic acid exts. of the tumors using dispersed rat adenohypophyseal cells in primary monolayer culture and a rat anterior pituitary perfusion system. The GH-releasing effect was dose-responsive and the greatest activity was present in the pancreatic islet tumor. Small amts. of activity were also found in 2 other tumors (carcinoid and small cell carcinoma of lung) unassociated with GH hypersecretion. Each of the tumors contained **somatostatin**-like immunoreactivity but the levels did not correlate with the net biologic expression of the tumor. Sephadex G-75 gel filtration indicated the GH-releasing activity has an apparent mol. size of slightly greater than 6,000 daltons. The GH-releasing activity was adsorbed onto DEAE-**cellulose** at neutral pH and low ionic strength, from which it could be eluted by increasing ionic strength. The GH-releasing activity was further purified by high pressure liq. chromatog. using an acetonitrile gradient on a cyanopropyl column to yield a prepn. that was active at 40 ng protein/mL. Partially purified

GH-releasing activity, from which most of the bioactive **somatostatin** had been removed, increased GH release by pituitary monolayer cultures to five times base line. Enzymic hydrolysis studies revealed that the GH-releasing activity was resistant to carboxypeptidase, leucineaminopeptidase, and pyroglutamate-aminopeptidase, but was destroyed by trypsin and chymotrypsin, indicating that internal lysine and/or arginine and arom. amino acid residues are required for biologic activity and that the NH2-terminus and COOH-terminus are either blocked or not essential. The results provide an explanation for the presence of GH-secreting tumors in some patients with the multiple endocrine neoplasia syndrome, type I, and warrant the addn. of GH-releasing activity to the growing list of hormones secreted by tumors of amine precursor uptake and decarboxylation cell types.

L3 ANSWER 49 OF 55 CAPLUS COPYRIGHT 2003 ACS
AN 1979:134707 CAPLUS
DN 90:134707
TI Development and validation of a specific radioimmunoassay for **somatostatin** in human plasma
AU Penman, Erica; Wass, J. A. H.; Lund, Alison; Lowry, P. J.; Stewart, Jennifer; Dawson, A. M.; Besser, G. M.; Rees, Lesley H.
CS Dep. Chem. Pathol., St. Bartholomew's Hosp., London, UK
SO Annals of Clinical Biochemistry (1979), 16(1), 15-25
CODEN: ACBOBU; ISSN: 0004-5632
DT Journal
LA English
AB A radioimmunoassay was developed and validated for **somatostatin** using prior extn. of the peptide onto leached silica glass. Tyrosine-11 **somatostatin** was iodinated using lactoperoxidase and purified on ODS silica. This method is superior to iodination using chloramine-T with CMC-**cellulose** purifn., and gives a highly purified prepn. with a shelf-life of at least 8 wks. Using this tracer and a specific antiserum, the limit of sensitivity of the assay was 10 pg/mL, with an intra-assay relative std. deviation of 12% (n = 16) and inter-assay relative std. deviation of 15% (n = 10). Parallelism was demonstrated between std. synthetic cyclic **somatostatin** and all extd. plasma samples. The mean recovery of exogenous **somatostatin** from plasma was 78%. The fasting level of immunoreactive **somatostatin** at 0900 h in normal subjects ranged from 17 to 81 pg/mL. Care is needed, however, when comparing these values with those obtained from other labs. since std. prepns. of **somatostatin** vary considerably in their immunopotency.

L3 ANSWER 50 OF 55 CAPLUS COPYRIGHT 2003 ACS
AN 1978:593414 CAPLUS
DN 89:193414
TI High molecular **somatostatin**. A possible interfering factor in radioimmunoassay
AU Diel, F.; Schneider, E.; Baumann, H.
CS Klin. Steglitz, Freie Univ. Berlin, Berlin, Fed. Rep. Ger.
SO Radioimmunoassay Relat. Proced. Med., Proc. Int. Symp. (1978), Meeting Date 1977, Volume 1, 123-32 Publisher: IAEA, Vienna, Austria.
CODEN: 39EEA2
DT Conference
LA English
AB Cyclic Tyr1-**somatostatin** (Tyr1-somatotropin-release-inhibiting factor, Tyr1-SRIF) was radioiodinated by the lactoperoxidase method. Purifn. was achieved by Sephadex G 25 chromatog. Specific anti-SRIF antiserum (FA1) was raised in rabbits. A dose-response curve was obtained in the range 5-5000 pg/tube using an antiserum diln. of 1:2000. There was little cross-reaction with linear **somatostatin**, and none with oxytocin, (Lys-, Arg-) vasopressin, valinomycin, polymyxin, insulin, glucagon, human growth hormones, LH-releasing hormone, and TSH-releasing hormone, each at a concn. of 10 mg/mL. The percentage of nonspecific

binding was 17% for a radioimmunoassay (RIA) incubation time of 18 h at 4.degree.. Bound and free antigen were sepd. by the charcoal technique. With the RIA described, no native cyclic SRIF could be measured in human plasma. For recovery tests, extn. procedures were necessary. Thin-layer chromatog. (TLC) and **polyacrylamide** gel disc electrophoresis (disc-PAGE) were performed to identify the presumed high-mol. 125I-Tyr1-SRIF associated material. This high-mol. wt. material may represent an interfering factor in the RIA for cyclic SRIF. Thus, the 1st elution peak, V0 (mol. wt. >5000), of the Sephadex G 25 chromatog. increased with storage time of the labeled Tyr1-SRIF. In the RIA, the nonspecific binding value increased from 17% to >30% B/T (bound/total) after a longer period of incubation. TLC of V0 and of the 125I-Tyr1-SRIF fractions from the retarded peak of the G 25 chromatog. shows similar Rf values in acidic elution systems. Disc-PAGE of 125I-Tyr1-SRIF demonstrated radioactivity in gel fractions corresponding to an Rf value of 0.35. This radioactivity could be extd. with acidic solvents.

L3 ANSWER 51 OF 55 CAPLUS COPYRIGHT 2003 ACS
AN 1978:593317 CAPLUS
DN 89:193317
TI Pig duodenal **somatostatin**: extraction and purification
AU Pradayrol, L.; Chayvialle, J.; Mutt, V.
CS Groupe Biol. Pathol. Dig., INSERM, Toulouse, Fr.
SO Metabolism, Clinical and Experimental (1978), 27(9, Suppl. 1), 1197-200
CODEN: METAAJ; ISSN: 0026-0495
DT Journal
LA English
AB **Somatostatin**-like immunoreactive (SLI) peptide was sepd. from pig duodenum, and some of its properties were compared with those of synthetic hypothalamic cyclic **somatostatin**. The isolation procedure includes: (a) gel filtration of a pig duodenal peptide conc. on Sephadex G 25 (10 .times. 100 cm) equilibrated with 0.2M HOAc; (b) ion-exchange chromatog. on a CM-**cellulose** column (1.5 .times. 19 cm) equilibrated with 0.1M NH4HCO3 (pH 7.9); (c) treatment of active fractions with alginic acid; and (d) rechromatog. on Sephadex G 25 (2 .times. 200 cm) equilibrated with 0.2M HOAc. Overall recovery of SLI material after these steps was 19%. The recovered SLI peptide was different from synthetic hypothalamic cyclic **somatostatin** as shown by gel filtration elution profile, hydrophobic chromatog. adsorption properties, and countercurrent distribution studies.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CAPLUS' ENTERED AT 16:44:58 ON 07 JUL 2003
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FILE COVERS 1907 - 7 Jul 2003 VOL 139 ISS 2
FILE LAST UPDATED: 6 Jul 2003 (20030706/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s somatostatin and ((anionic polymer) or polyacrylamide or polysaccharide or starch or cellulose) and patent/dt

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         16999 SOMATOSTATIN
           133 SOMATOSTATINS
         17007 SOMATOSTATIN
                 (SOMATOSTATIN OR SOMATOSTATINS)
         98673 ANIONIC
           239 ANIONICS
         98767 ANIONIC
                 (ANIONIC OR ANIONICS)
        904013 POLYMER
        763750 POLYMERS
       1233056 POLYMER
                 (POLYMER OR POLYMERS)
          2396 ANIONIC POLYMER
                 (ANIONIC(W)POLYMER)
         84745 POLYACRYLAMIDE
          1570 POLYACRYLAMIDES
         85168 POLYACRYLAMIDE
                 (POLYACRYLAMIDE OR POLYACRYLAMIDES)
         49638 POLYSACCHARIDE
         60530 POLYSACCHARIDES
         77263 POLYSACCHARIDE
                 (POLYSACCHARIDE OR POLYSACCHARIDES)
        134230 STARCH
          7901 STARCHES
        135231 STARCH
                 (STARCH OR STARCHES)
        304862 CELLULOSE
          3998 CELLULOSES
        305394 CELLULOSE
                 (CELLULOSE OR CELLULOSES)
       4131129 PATENT/DT
L1           82 SOMATOSTATIN AND ((ANIONIC POLYMER) OR POLYACRYLAMIDE OR POLYSAC
                CHARIDE OR STARCH OR CELLULOSE) AND PATENT/DT
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=> s l1 and (SUSPENSION OR SOLUTION OR FORMULATION)
         182421 SUSPENSION
          81550 SUSPENSIONS
         231985 SUSPENSION
                (SUSPENSION OR SUSPENSIONS)
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         255667 SOLUTIONS
         463346 SOLUTION
                (SOLUTION OR SOLUTIONS)
        1994120 SOLN
         938060 SOLNS
        2526065 SOLN
                (SOLN OR SOLNS)
        2626409 SOLUTION
                (SOLUTION OR SOLN)
         108652 FORMULATION
          72496 FORMULATIONS
         160337 FORMULATION
                (FORMULATION OR FORMULATIONS)
L2           35 L1 AND (SUSPENSION OR SOLUTION OR FORMULATION)

=> d bib,kwic 20,24,27,29,32,33,34

L2   ANSWER 20 OF 35  CAPLUS  COPYRIGHT 2003 ACS
AN   1998:509085  CAPLUS
DN   129:127192
TI   Preparation of particles for inhalation
IN   Edwards, David A.; Hanes, Justin; Evora, Carmen; Langer, Robert S.;
     Vanbever, Rita; Mintzes, Jeffrey; Wang, Jue; Chen, Donghao
PA   Massachusetts Institute of Technology, USA; The Penn State Research
     Foundation
SO   PCT Int. Appl., 64 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 5
     PATENT NO.         KIND  DATE           APPLICATION NO.  DATE
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PI   WO 9831346         A1    19980723       WO 1997-US20930  19971117
         W:  CA, JP
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     US 5855913         A     19990105       US 1997-784421   19970116
     CA 2403349         AA    19980723       CA 1997-2403349  19971117
     EP 954282          A1    19991110       EP 1997-947545   19971117
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     JP 2001526634      T2    20011218       JP 1998-534332   19971117
     CA 2277801         C     20021015       CA 1997-2277801  19971117
     US 2003068277      A1    20030410       US 2002-94955    20020307
PRAI US 1997-784421     A     19970116
     US 1997-59004P     P     19970915
     CA 1997-2277801    A3    19971117
     US 1997-971791     A2    19971117
     WO 1997-US20930    W     19971117
     US 1999-394233     A2    19990913
     US 2001-909145     B1    20010719
RE.CNT  7     THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
DT   Patent
AB   Particles incorporating a surfactant and/or a hydrophilic or hydrophobic
     complex of a pos. or neg. charged therapeutic agent and a charged mol. of
     opposite charge for drug delivery to the pulmonary system, and methods for
     their synthesis and administration are provided.  In a preferred
     embodiment, the particles are made of a biodegradable material and have a
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tap d. less than 0.4 g/cm3 and a mass mean diam. 5-30 .mu.m, which together yield an aerodynamic diam. of the particles of 1-3 .mu.m. The particles may be formed of biodegradable materials such as biodegradable polymers. For example, the particles may be formed of poly(lactic acid) or poly(glycolic acid) or copolymers thereof. Alternatively, the particles may be formed solely of a therapeutic or diagnostic agent and a surfactant. Surfactants can be incorporated on the particle surface for example by coating the particle after particle formation, or by incorporating the surfactant in the material forming the particle prior to formation of the particle. Exemplary surfactants include phosphoglycerides such as dipalmitoyl phosphatidylcholine (DPPC). The particles can be effectively aerosolized for administration to the respiratory tract to permit systemic or local delivery of wide a variety of therapeutic agents. Formation of complexes of pos. or neg. charged therapeutic agents with mols. of opposite charge can allow control of the release rate of the agents into the blood stream following administration. Porous particles were prepd. by spray drying a **soln.** contg. insulin 2, albumins 19, lactose 19, and dipalmitoylphosphatidylcholine 60 %.

IT Albumins, biological studies
Lipids, biological studies
Nucleic acids
Nucleotides, biological studies
Oligonucleotides
Polysaccharides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (particulate compns. contg. therapeutic agents and surfactants for inhalation)

IT 50-28-2, Estradiol, biological studies 51-34-3, Scopolamine 54-11-5, Nicotine 57-83-0, Progesterone, biological studies 58-22-0, Testosterone 68-22-4, Norethindrone 69-72-7, biological studies 437-38-7, Fentanyl 439-14-5, Valium 4205-90-7, Clonidine 9004-10-8, Insulin, biological studies 9004-17-5, Zinc protamine insulin 9007-12-9, Calcitonin 15826-37-6, Cromolyn sodium 18559-94-9, Albuterol 51110-01-1, **Somatostatin** 53714-56-0, Leuprolide 89365-50-4, Salmeterol 103370-86-1, Parathyroid hormone-related peptide 143011-72-7, Granulocyte colony-stimulating factor
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (particulate compns. contg. therapeutic agents and surfactants for inhalation)

L2 ANSWER 24 OF 35 CAPLUS COPYRIGHT 2003 ACS
AN 1996:483651 CAPLUS
DN 125:123755
TI Aerosol **formulations** of peptides and proteins
IN Baeckstroem, Kjell; Dahlbaeck, Magnus; Johansson, Ann; Kaellstrand, Goeran; Lindqvist, Elisabet
PA Astra Aktiebolag, Swed.; Kaellstrand, Goeran
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9619197	A1	19960627	WO 1995-SE1540	19951219
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9510752	A	19960624	ZA 1995-10752	19951218

	CA 2206736	AA	19960627	CA 1995-2206736	19951219
	AU 9643591	A1	19960710	AU 1996-43591	19951219
	AU 702879	B2	19990311		
	EP 797431	A1	19971001	EP 1995-942341	19951219
	EP 797431	B1	20020522		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, LT, LV				
	BR 9510501	A	19980113	BR 1995-10501	19951219
	CN 1171046	A	19980121	CN 1995-196977	19951219
	CN 1088581	B	20020807		
	HU 77701	A2	19980728	HU 1998-560	19951219
	JP 10510827	T2	19981020	JP 1995-519730	19951219
	TW 398978	B	20000721	TW 1995-84113556	19951219
	IL 116458	A1	20010111	IL 1995-116458	19951219
	CZ 288145	B6	20010516	CZ 1997-1945	19951219
	RU 2175866	C2	20011120	RU 1997-112497	19951219
	PL 182560	B1	20020131	PL 1995-320824	19951219
	EE 3590	B1	20020215	EE 1997-137	19951219
	EP 1180365	A2	20020220	EP 2001-127823	19951219
	EP 1180365	A3	20030625		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, LT, LV				
	AT 217787	E	20020615	AT 1995-942341	19951219
	ES 2176355	T3	20021201	ES 1995-942341	19951219
	US 6524557	B1	20030225	US 1996-624504	19960405
	NO 9702781	A	19970616	NO 1997-2781	19970616
	FI 9702657	A	19970619	FI 1997-2657	19970619
PRAI	SE 1994-4467	A	19941222		
	SE 1995-2453	A	19950706		
	EP 1995-942341	A3	19951219		
	WO 1995-SE1540	W	19951219		

TI Aerosol **formulations** of peptides and proteins

DT **Patent**

AB A pharmaceutical aerosol **formulation** comprises (a) a hydrofluoroalkane propellant; (b) a pharmaceutically active polypeptide dispersible in the propellant; and (c) a surfactant which is a C8-C16 fatty acid or salt thereof, a bile salt, a phospholipid, or an alkyl saccharide, which surfactant enhances the systemic absorption of the polypeptide in the lower respiratory tract. Na caprate 25 parts and insulin 75 parts were micronized sep. and the mixt. was added to a bottle, which was chilled to -40.degree. and chilled 1,1,1,2-tetrafluoroethane was added. The bottle was sealed with a metering valve and then shaken vigorously for 30 s to give a good **suspension**.

ST aerosol protein hydrofluoroalkane propellant surfactant; insulin caprate tetrafluoroethane **suspension** aerosol

IT Albumins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(additive; aerosol **formulations** of peptides and proteins)

IT Gonadotropins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aerosol **formulations** of peptides and proteins)

IT Bile salts
Lysophosphatidylcholines
Lysophosphatidylethanolamines
Lysophosphatidylglycerols
Monosaccharides
Phosphatidylinositols
Phosphatidylserines
Phospholipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surfactants; aerosol **formulations** of peptides and proteins)

IT Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C8-16, surfactants; aerosol **formulations** of peptides and

proteins)
IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biol. active, aerosol **formulations** of peptides and proteins)
IT Pharmaceutical dosage forms
(sprays, aerosol **formulations** of peptides and proteins)
IT 50-99-7, Glucose, biological studies 56-40-6, Glycine, biological studies 56-41-7, Alanine, biological studies 57-48-7, Fructose, biological studies 57-50-1, biological studies 59-23-4, Galactose, biological studies 63-42-3 69-65-8, D-Mannitol 69-79-4 87-89-8, Myoinositol 87-99-0, Xylitol 99-20-7, Trehalose 107-43-7, Betaine 470-55-3 512-69-6 585-86-4, Lactitol 585-88-6, Maltitol 597-12-6, Melezitose 9005-25-8, **Starch**, biological studies 64519-82-0, Palatinit
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(additive; aerosol **formulations** of peptides and proteins)
IT 50-56-6, Oxytocin, biological studies 75-37-6, 1,1-Difluoroethane 145-42-6, Sodium taurocholate 361-09-1, Sodium cholate 431-89-0, 1,1,1,2,3,3,3-Heptafluoropropane 629-25-4, Sodium laurate 811-97-2, 1,1,1,2-Tetrafluoroethane 822-12-8, Sodium myristate 863-57-0, Sodium glycocholate 1002-62-6, Sodium caprate 5593-79-3, Potassium cholate 7487-77-6, Potassium taurocholate 9002-60-2, Corticotropin, biological studies 9002-64-6, Parathyroid hormone 9002-68-0, Follicle-stimulating hormone 9002-72-6, Growth hormone 9003-98-9, DNase 9004-10-8, Insulin, biological studies 9007-12-9, Calcitonin 9007-92-5, Glucagon, biological studies 9015-71-8, Corticotropin-releasing hormone 9034-39-3, Growth hormone-releasing factor 9034-40-6, Gonadotropin-releasing hormone 10124-65-9, Potassium laurate 11000-17-2, Vasopressin 13040-18-1, Potassium caprate 13429-27-1, Potassium myristate 14479-93-7, Lysine laurate 16679-58-6, Desmopressin 24305-27-9, Thyrotropin-releasing hormone 40111-13-5, Potassium glycocholate 41017-85-0, Dioctanoylphosphatidylcholine 51110-01-1, **Somatostatin** 58846-77-8, Decyl glucoside 62470-55-7 69227-93-6 85637-73-6, Atrial natriuretic factor 118353-07-4 179560-07-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aerosol **formulations** of peptides and proteins)
IT 764-71-6, Potassium caprylate 1984-06-1, Sodium caprylate 118353-06-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surfactant; aerosol **formulations** of peptides and proteins)

L2 ANSWER 27 OF 35 CAPLUS COPYRIGHT 2003 ACS
AN 1994:541739 CAPLUS
DN 121:141739
TI Pharmaceutical nanocapsules for oral administration of peptides and **polysaccharides** comprising poly(C1-6 alkyl-2-cyanoacrylates)
IN Vranckx, Henri; Demoustier, Martine; Deleers, Michel
PA U C B, S.A., Belg.
SO Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DT **Patent**
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 608207	A1	19940727	EP 1994-870001	19940105
EP 608207	B1	19981014		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 172111	E	19981015	AT 1994-870001	19940105
ES 2122217	T3	19981216	ES 1994-870001	19940105
US 5500224	A	19960319	US 1994-179205	19940110
PL 173254	B1	19980227	PL 1994-301841	19940110
CA 2113243	AA	19940719	CA 1994-2113243	19940111
FI 9400115	A	19940719	FI 1994-115	19940111

	AU 9453097	A1	19940721	AU 1994-53097	19940111
	AU 670840	B2	19960801		
	NO 9400111	A	19940719	NO 1994-111	19940112
	ZA 9400205	A	19940822	ZA 1994-205	19940112
	JP 06256172	A2	19940913	JP 1994-1830	19940113
	RU 2145498	C1	20000220	RU 1994-2474	19940113
	HU 67213	A2	19950328	HU 1994-107	19940114
PRAI	GB 1993-875	A	19930118		

TI Pharmaceutical nanocapsules for oral administration of peptides and **polysaccharides** comprising poly(C1-6 alkyl-2-cyanoacrylates)

DT **Patent**

AB Pharmaceutical nanocapsules for oral administration of peptides and **polysaccharides** comprising poly(C1-6 alkyl-2-cyanoacrylates) with diam. .ltoreq.500 nm are disclosed. Thus, 1 mL Na lauryl sulfate 5% in acetate buffer was stirred with 10 mL Miglyol 812 contg. 15% Span 80 and the **suspension** was added to 100.mu.L of butyl-2-cyanoacrylate and left for 240 min to polymerize. The nanocapsules thus obtained were stable for 18 mo at 4.degree..

ST nanocapsule oral peptide **polysaccharide** alkyl cyanoacrylate

IT **Polysaccharides**, biological studies
RL: BIOL (Biological study)
(pharmaceutical nanocapsules for oral administration of peptides and, comprising poly(C1-6 alkylcyanoacrylates))

IT Peptides, biological studies
RL: BIOL (Biological study)
(pharmaceutical nanocapsules for oral administration of **polysaccharides** and, comprising poly(C1-6 alkylcyanoacrylates))

IT Pharmaceutical dosage forms
(nanocapsules, for oral administration of peptides and **polysaccharides**, comprising poly(C1-6 alkylcyanoacrylates))

IT 8049-62-5, Zinc insulin 9004-10-8, Insulin, biological studies 9007-12-9, Calcitonin 51110-01-1, **Somatostatin**
RL: BIOL (Biological study)
(pharmaceutical nanocapsules for oral administration of **polysaccharides** and, comprising poly(C1-6 alkylcyanoacrylates))

L2 ANSWER 29 OF 35 CAPLUS COPYRIGHT 2003 ACS

AN 1993:109720 CAPLUS

DN 118:109720

TI Oral and buccal pharmaceutical composition containing polypeptides and promotion enhancers

IN Takama, Shigeyuki; Inamoto, Yukiko; Wato, Takahiko; Yamada, Akiya; Uchida, Naoki; Kadoriku, Misuzu

PA Teikoku Seiyaku K. K., Japan

SO Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW

DT **Patent**

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 517211	A1	19921209	EP 1992-109453	19920604
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
	CA 2070061	AA	19921208	CA 1992-2070061	19920529
	AU 9217264	A1	19921210	AU 1992-17264	19920529
	AU 653026	B2	19940915		
	JP 05148154	A2	19930615	JP 1992-138518	19920529
	JP 3253127	B2	20020204		
	NO 9202232	A	19921208	NO 1992-2232	19920605
	US 5929027	A	19990727	US 1997-815574	19970312
PRAI	JP 1991-136462	A	19910607		
	US 1992-893575	B1	19920604		
	US 1994-262362	B3	19940620		

DT **Patent**

AB The title compn. comprises a polypeptide, an absorption promoting agent consisting of a combination of an org. acid and a fatty acid sucrose ester in admixt. with a carrier or diluent, which is suitable for oral administration and for application to the oral cavity. A sublingual tablet contained lactose 58.8, cryst. **cellulose** 24, polyvinylpyrrolidone 3, sucrose palmitate 4, malic acid 10, human calcitonin 0.2g.

IT Pharmaceutical dosage forms
(**solns**., peptides and absorption enhancers in)

IT 50-56-6, Oxytocin, biological studies 1393-25-5, Secretin 1407-47-2, Angiotensin 9002-60-2, ACTH, biological studies 9002-64-6, Parathyroid hormone 9002-71-5, Thyrotropin 9002-76-0, Gastrin 9002-79-3, Melanotropin 9007-12-9, Calcitonin 9007-92-5, Glucagon, biological studies 9038-70-4, Somatomedin 24305-27-9, TRH 25126-32-3 37221-79-7, Vasoactive intestinal peptide 39379-15-2, Neurotensin 51110-01-1, **Somatostatin** 60617-12-1, .beta.-Endorphin 80043-53-4, Gastrin-releasing peptide 83652-28-2, Calcitonin gene related peptide 85637-73-6, Atriopeptin 116243-73-3, Endothelin
RL: BIOL (Biological study)
(oral and buccal pharmaceutical compn. contg. absorption enhancers and)

L2 ANSWER 32 OF 35 CAPLUS COPYRIGHT 2003 ACS
AN 1992:91416 CAPLUS
DN 116:91416
TI Pharmaceutical resorption-improved **somatostatin** compositions
IN Fricker, Gerd; Vonderscher, Jacky
PA Sandoz A.-G., Switz.
SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 462071	A1	19911218	EP 1991-810450	19910613
	EP 462071	B1	19950201		
	R: BE, DK, ES, GR, NL, SE				
	HU 59007	A2	19920428	HU 1991-1849	19910603
	DE 4119062	A1	19911219	DE 1991-4119062	19910610
	GB 2244918	A1	19911218	GB 1991-12509	19910611
	GB 2244918	B2	19940615		
	CH 683069	A	19940114	CH 1991-1755	19910612
	NO 9102271	A	19911216	NO 1991-2271	19910613
	CA 2044511	AA	19911216	CA 1991-2044511	19910613
	FI 9102868	A	19911216	FI 1991-2868	19910613
	AU 9178331	A1	19920102	AU 1991-78331	19910613
	ES 2067906	T3	19950401	ES 1991-810450	19910613
	FR 2663227	A1	19911220	FR 1991-7345	19910614
	FR 2663227	B1	19950428		
	JP 04230223	A2	19920819	JP 1991-143095	19910614
	ZA 9104583	A	19930224	ZA 1991-4583	19910614
	FR 2668933	A1	19920515	FR 1991-15570	19911119
	FR 2668933	B1	19950505		
PRAI	GB 1990-13448		19900615		

TI Pharmaceutical resorption-improved **somatostatin** compositions
DT **Patent**
AB A **somatostatin**-contg. compn. for the administration via a transmucosal route comprises ursodeoxycholic acid or chenodeoxycholic acid as a resorption promoter having the inhibitory activity of gallstone formation induced by **somatostatin** as a side effect. When the compn. is administered to the jejunum of the rat, a relative **somatostatin** bioavailability is enhanced by .gtoreq.400 %, compared with the same compns. without the resorption promoter. An oral capsule contained octreotide 2.3 (equiv. to 2 mg **somatostatin**),

chenodeoxycholic acid 150, microcryst. **cellulose** 100, and lactose 50 mg.

ST **somatostatin** capsule ursodeoxycholate absorption promoter; octreotide chenodeoxycholate capsule

IT Calculi, biliary
(formation of, induced by **somatostatin**, cholanic acids effect on)

IT Drug bioavailability
(of **somatostatin**, from chenodeoxycholate-contg. **solns**.)

IT Pharmaceutical dosage forms
(capsules, of **somatostatin**, cholanic acids as absorption promoters in)

IT Pharmaceutical dosage forms
(mucosal, of **somatostatin**, cholanic acids as absorption promoters in)

IT Pharmaceutical dosage forms
(nasal, of **somatostatin**, cholanic acids as absorption promoters in)

IT Pharmaceutical dosage forms
(oral, of **somatostatin**, cholanic acids as absorption promoters in)

IT Pharmaceutical dosage forms
(rectal, of **somatostatin**, cholanic acids as absorption promoters in)

IT Pharmaceutical dosage forms
(suppositories, of **somatostatin**, cholanic acids as absorption promoters in)

IT 128-13-2, Ursodeoxycholic acid 474-25-9, Chenodeoxycholic acid
RL: BIOL (Biological study)
(**somatostatin** transmucosal **formulations** contg., as absorption promoter)

IT 83150-76-9, Octreotide
RL: BIOL (Biological study)
(transmucosal **formulations** of, chenodeoxycholate as absorption promoter in)

IT 51110-01-1, **Somatostatin**
RL: BIOL (Biological study)
(transmucosal **formulations** of, cholanic acids as absorption promoters in)

L2 ANSWER 33 OF 35 CAPLUS COPYRIGHT 2003 ACS

AN 1991:49597 CAPLUS

DN 114:49597

TI Process for microencapsulation of bioactive substances in polymers

IN Komen, Joseph; Groenendaal, Jan Willem

PA Gist-Brocades N. V., Neth.

SO Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW

DT **Patent**

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 377477	A1	19900711	EP 1990-200006	19900102
	EP 377477	B1	19930324		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL				
	IL 92344	A1	19930513	IL 1989-92344	19891117
	US 5066436	A	19911119	US 1989-457257	19891227
	JP 02247117	A2	19901002	JP 1989-339901	19891228
	AU 9047397	A1	19900712	AU 1990-47397	19900102
	AU 622967	B2	19920430		
	AT 87235	E	19930415	AT 1990-200006	19900102
	ES 2055292	T3	19940816	ES 1990-200006	19900102

PRAI EP 1989-200015 19890104
EP 1990-200006 19900102

DT **Patent**

AB A process for microencapsulating bioactive substances in biocompatible polymers according to the phase sepn. principle for the prodn. of controlled-release prepns. comprises, (1) dispersing the bioactive substance in an org. **soln**. of a biocompatible polymer, (2) adding to the dispersion a coacervation agent, (3) adding an excess of a hardening liq., and (4) collecting, washing, and drying the microcapsules. The hardening liq. is an Et or isopropyl ester of a straight-chain C12-18 fatty acid. The microcapsules are dispersed in a suitable carrier for parenteral and oral administration. A 10% **soln**. of DL-lactide-glycolide copolymer in CH2Cl2 100 mL was added to 800 mg of bovine serum albumin with stirring and 50 mL of silicone oil was added; the whole content was then poured into 2000 mL of isopropyl myristate at 5.degree. and the obtained microcapsules were washed and sieved; the size of the microcapsules was 25-140 .mu.m and the amt. of the albumin in the microcapsules was 4.73%. The above microcapsules were placed in a phosphate buffer to det. the release of the albumin; an approx. linear release of the albumin up to 70% after 28 days was obsd.

IT 9004-38-0, **Cellulose** acetate phthalate 9004-57-3, Ethyl **cellulose** 9050-31-1 26023-30-3 26161-42-2 26589-39-9, Eudragit S 26680-10-4, Poly(DL-lactide) 26780-50-7, DL-Lactide-glycolide copolymer 33135-50-1, Poly(L-lactide) 33434-24-1, Eudragit RL 51822-44-7, Eudragit L 52907-01-4, **Cellulose** acetate trimellitate 53237-50-6 125053-52-3, Eudragit NE 300
RL: BIOL (Biological study)
(bioactive compd. microencapsulation with)

IT 50-56-6, Oxytocin, biological studies 65-49-6, 4-Aminosalicylic acid 89-57-6, 5-Aminosalicylic acid 1407-47-2D, Angiotensin, analogs 5534-09-8, Beclomethasone 17,21-dipropionate 9002-60-2D, Adrenocorticotrophic hormone, analogs 9002-64-6D, Parathyroid hormone, analogs 9002-72-6D, Growth hormone, analogs 9002-76-0D, Gastrin, analogs 9004-10-8D, Insulin, analogs 9007-12-9D, Calcitonin, analogs 9015-71-8D, Corticotropin-releasing factor, analogs 11000-17-2D, Vasopressin, analogs 51110-01-1, **Somatostatin** 57644-54-9, Bismuth subcitrate 59392-49-3D, Gastric inhibitory peptide, analogs 60118-07-2D, Endorphin, analogs 80043-53-4D, Gastrin releasing peptide, analogs
RL: BIOL (Biological study)
(microencapsulation of, in polymers, fatty acid ester hardening agents for)

L2 ANSWER 34 OF 35 CAPLUS COPYRIGHT 2003 ACS
AN 1990:62633 CAPLUS
DN 112:62633
TI Intranasal administration of polypeptides in powdered form
IN Vickery, Brian H.; Fu, Cherng Chyi; Benjamin, Eric J.; Sanders, Lynda M.
PA Syntex (U.S.A.), Inc., USA
SO Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 312052	A1	19890419	EP 1988-117029	19881013
EP 312052	B1	19940105		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 01132532	A2	19890525	JP 1988-260350	19881013
JP 2851627	B2	19990127		
ZA 8807658	A	19900627	ZA 1988-7658	19881013
AT 99543	E	19940115	AT 1988-117029	19881013
ES 2061591	T3	19941216	ES 1988-117029	19881013

	CA 1336401	A1	19950725	CA 1988-580103	19881013
	AU 8823751	A1	19890601	AU 1988-23751	19881014
	AU 623609	B2	19920521		
	US 6521597	B1	20030218	US 1992-902405	19920619
PRAI	US 1987-109678	A	19871015		
	EP 1988-117029	A	19881013		

DT **Patent**

AB Pharmaceutical powders for intranasal administration comprise biol. active polypeptides, e.g. LHRH analogs, or their salts and water-sol. **polysaccharides**. A powd. **formulation** having 4 wt.% nafarelin (I) and 2 wt.% Na glycocholate (absorption enhancer) was made by freeze-drying a **soln**. contg. I acetate in an amt. equiv. to 10 mg I as the free base, 235 mg dextran T70 and 5 mg Na glycocholate, grinding the product and passing the resultant powder through a #200 std. mesh. The peak blood level in monkeys of I was 76 ng/mL from a 100 mg dose of the above **formulation** (400 .mu.g I) compared with 22 ng/mL from a 4% powder without the absorption enhancer and 8 ng/mL from a nasal **soln**.

ST polypeptide **polysaccharide** nasal powder; peptide **polysaccharide** nasal powder

IT Peptides, biological studies
RL: BIOL (Biological study)
(bioactive, nasal powders contg. water-sol. **polysaccharides** and)

IT **Polysaccharides**, biological studies
RL: BIOL (Biological study)
(nasal powders contg. bioactive polypeptides and)

IT Pharmaceutical dosage forms
(powders, nasal, contg. bioactive polypeptides and water-sol. **polysaccharides**)

IT 9002-64-6, Parathyroid hormone 9015-71-8, Corticotropin-releasing factor 9034-39-3, GHRH 40958-31-4, **Somatostatin** (sheep reduced) 53714-56-0, Leuprorelin 57773-63-4 57773-65-6 57982-77-1, Buserelin 65807-02-5, Goserelin 66866-63-5, Lutrelin 76712-82-8, Histrelin 76932-56-4, Nafarelin 76932-60-0, Nafarelin acetate 85637-73-6, Atrial natriuretic peptide 89662-30-6, Detirelix 91991-07-0 124904-93-4 124926-38-1
RL: BIOL (Biological study)
(nasal powders contg. dextran and)